Glucosamine and chondroitin Research

Glucosamine is a popular over-the-counter supplement that appeals to older people suffering with arthritic pain and sports enthusiasts.

Users typically suffer chronic pain caused by joint trauma (meniscal tears or other knee damage) and also those who expose their knees to potential risk who wish to reduce or avoid joint damage.

Glucosamine and chondroitin are frequently used in combination are on the “alternative” medications list, as there was no conclusive evidence that it works. At the end of 2005 a US government research team announced the results of a huge controlled trial undertaken in 2000.

The answers about glucosamine are contained in the study posted by the National Institutes of Health, The National Center for Complementary and Alternative Medicine (NCCAM) web site: http://nccam.nih.gov/research/results/gait/qa.htm

Questions and Answers: NIH Glucosamine/chondroitin Arthritis Intervention Trial Primary Study

• About the Study
  o What is the Glucosamine/chondroitin Arthritis Intervention Trial (GAIT)?
  o What was the purpose of the study?
  o What was the basic design of the study?
  o What did GAIT cost?

• Study Background
  o What is osteoarthritis?
  o What are glucosamine and chondroitin sulfate?
  o What is celecoxib?
  o What doses were used for the various treatments?
  o Who provided the source materials for making the glucosamine and chondroitin sulfate products used in GAIT?
  o Where did the other study products come from?
  o Where was the study conducted?

• Key Results
  o What were the key results of the study?
  o How many people participated in the study and who were they?
  o Were there any side effects from the treatments?

• Consumer Information and Next Steps
  • Should people with osteoarthritis use glucosamine and chondroitin sulfate?
  o Can U.S. consumers get the glucosamine and chondroitin sulfate products used in GAIT?
  o Did the GAIT team do any additional research on glucosamine and chondroitin sulfate?

For More Information About the Study

What is the Glucosamine/chondroitin Arthritis Intervention Trial (GAIT)?

GAIT is the first large-scale, multicenter clinical trial in the United States to test the effects of the dietary supplements glucosamine hydrochloride (glucosamine) and sodium chondroitin sulfate (chondroitin sulfate) for the treatment of knee osteoarthritis. The study tested whether glucosamine and chondroitin sulfate used separately or in combination reduced pain in participants with knee osteoarthritis.

The University of Utah, School of Medicine coordinated this study, which was conducted at 16 rheumatology research centers across the United States. The National Center for Complementary and Alternative Medicine (NCCAM) and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), two components of the National Institutes of Health (NIH), funded GAIT.

What was the purpose of the study?

Previous studies in the medical literature had conflicting results on the effectiveness of glucosamine and chondroitin sulfate as treatments for osteoarthritis. GAIT was designed to test the short-term (6 months) effectiveness of glucosamine and chondroitin sulfate in reducing pain in a large number of participants with knee osteoarthritis.

The basic design of the study -

In GAIT, participants were randomly assigned to one of five treatment groups:
(1) glucosamine alone
(2) chondroitin sulfate alone
(3) glucosamine and chondroitin sulfate in combination
(4) celecoxib
(5) a placebo (an inactive substance that looks like the study substance).

Glucosamine and chondroitin sulfate and their combination were compared with a placebo to evaluate whether these substances significantly improve joint pain. Celecoxib, which is a prescription drug effective in managing osteoarthritis pain, was also compared with placebo to validate the study design.
To reduce the chance of biased results, the study was double-blinded—neither the researchers nor the participants knew which of the five treatment groups the participants were in. Participants received treatment for 24 weeks.

Participants were evaluated at the start of the study and at weeks 4, 8, 16, and 24 and closely monitored for improvement of their symptoms as well as for any possible adverse reactions to the study agents. X-rays documented each participant’s diagnosis of osteoarthritis.

Participants were also stratified into two pain subgroups—1,229 participants (78 percent) with mild pain and 354 participants (22 percent) with moderate-to-severe pain.

A positive response to treatment was defined as a 20 percent or greater reduction in pain at week 24 compared to the start of the study. All participants had the option to use up to 4000 mg of acetaminophen, as needed, to control pain from osteoarthritis throughout the study, except for the 24 hours prior to having their knee assessed.

Acetaminophen use was low: on average, participants used fewer than two 500 mg tablets per day.

**What did GAIT cost?**

The primary GAIT study cost just over $12.5 million.

**Study Background**

**What is osteoarthritis?**

An estimated 27 million adults in the United States live with osteoarthritis—the most common type of arthritis. Osteoarthritis, also called degenerative joint disease, is caused by the breakdown of cartilage, which is the connective tissue that cushions the ends of bones within the joint.

Osteoarthritis is characterized by pain, joint damage, and limited motion. The disease generally occurs late in life, and most commonly affects the hands and large weight-bearing joints, such as the knees. Age, female gender, and obesity are risk factors for this condition.

Illustrations of a Joint with Osteoarthritis and a health joint

Image provided by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

**What are glucosamine and chondroitin sulfate?**

Glucosamine and chondroitin sulfate are natural substances found in and around the cells of cartilage. Glucosamine is an amino sugar that the body produces and distributes in cartilage and other connective tissue, and chondroitin sulfate is a complex carbohydrate that helps cartilage retain water.
In the United States, glucosamine and chondroitin sulfate are sold as dietary supplements, which are regulated as foods rather than drugs.

**What is celecoxib?**

Celecoxib (brand name Celebrex) is a type of nonsteroidal anti-inflammatory drug (NSAID), called a COX-2 inhibitor. Like traditional NSAIDs, celecoxib blocks the COX-2 enzyme in the body that stimulates inflammation.

Unlike traditional NSAIDs, however, celecoxib does not block the action of COX-1 enzyme, which is known to protect the stomach lining. As a result, celecoxib reduces joint pain and inflammation with reduced risk of gastrointestinal ulceration and bleeding.

Recent reports have linked possible cardiovascular side effects to COX-2 inhibitors. Although GAIT was not designed to study the safety of celecoxib, participants were monitored for adverse events and no increase in such side effects was observed.

**What doses were used for the various treatments?**

The doses used in GAIT were based on the doses seen in the prevailing scientific literature:

- Glucosamine alone: 1500 mg daily given as 500 mg three times a day
- Chondroitin sulfate alone: 1200 mg daily given as 400 mg three times a day
- Glucosamine plus chondroitin sulfate combined: same doses-1500 mg and 1200 mg daily
- Celecoxib: 200 mg daily
- Acetaminophen: participants were allowed to take up to 4000 mg (500 mg tablets) per day to control pain, except for the 24 hours before pain was assessed.

**Who provided the source materials for making the glucosamine and chondroitin sulfate products used in GAIT?**

- Glucosamine was donated in part by Ferro Pfanstiehl Laboratories, Inc., Waukegan, IL, through Wilke Resources.
- Chondroitin sulfate was donated by Bioiberica, S.A., Barcelona, Spain.

The study agents were manufactured by Albuquerque Veterans Affairs (VA) Cooperative Studies Program Clinical Research Pharmacy.

**Where did the other study products come from?**

- Acetaminophen was donated by McNeil Consumer and Specialty Pharmaceuticals, Fort Washington, PA.
- Celecoxib was purchased from Pfizer.